UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,632	01/14/2004	Bianca Baroli	0492611-0520	4661

24280 7590 07/10/2007

CHOATE, HALL & STEWART LLP
TWO INTERNATIONAL PLACE
BOSTON, MA 02110

EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	**PAPER NUMBER**
1651	
MAIL DATE	**DELIVERY MODE**
07/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/757,632	BAROLI ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *2,4,5,7-11,13-20,24,34-38,40-47,51 and 60-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6,12,21-23,25-33,39,48-50 and 52-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/19/04, 1/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

Applicant's amendments filed 4/23/07 to claims 22, 26, 28, 29, 31, 49, 53, 55-57, 59, 61, 74, 80, and 81 have been entered. No claims have been cancelled or added. Claims 1-81 remain pending in the current application.

Election/Restrictions

Applicant's election with traverse of the species "tissue engineering," "gelatin," "protein," "sugar," "polyethylene glycol," "cross-linked synthetic polymer," "granulation," "visible radiation," and "dissolution-controlled systems" in the reply filed on 4/23/07 is acknowledged. The traversal is on the ground(s) that it would not be burdensome for the examiner to search all of the species within the scope of the generic claims (Remarks, page 9, last paragraph). This is not found persuasive because the sheer number of species would cause a serious burden to the examiner. Applicant has provided no evidence that the species in each genus set forth in the restriction are obvious over each other, so a text search of each and every species in each and every dependent claim would be required. Such a search would certainly be burdensome, since the claims recite nearly 200 individual species, each of which would require a separate text search in patent and non-patent databases.

Applicant's allegations that the species "granules" is not distinct from "capsules;" that "stem cells," "human cells," and "animal cells" are not distinct from each other; that "nanoparticles," "nanospheres," and "solid lipid nanoparticles" are not distinct from each other; and that "microparticles" and "microspheres" are not distinct from each other are

confusing. First, these allegations are not supported by evidence that the species are obvious over each other. Second, none of these species are among those elected by applicant. The examiner agrees, however, that the species of sugars recited in claims 23, 50, and 75 are not distinct from the elected binder, "sugars."

The requirement is still deemed proper and is therefore made FINAL.

Claims 2, 4, 5, 7-11, 13-20, 24, 34-38, 40-47, 51, and 60-81 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim[1]. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/23/07.

The examiner wishes to point out for the record that an election of species requirement is for search purposes only and does not necessarily narrow the scope of patentable claims, since all nonelected species will bee rejoined at the time of allowance. See 37 C.F.R. §1.146 and M.P.E.P. § 809.02(c) for a discussion of species election practice. In short, electing one species does not preclude consideration of the nonelected species later in the prosecution, *i.e.* at the time of allowance. In the interest of expedient processing of applications, the examiner concentrates on the patentability of the entire invention as it pertains to one species. Once the invention *per se* is claimed in an allowable manner, all allowable disclosed species will be rejoined to the claims.

Examination on the merits will commence at this time on claims 1, 3, 6, 12, 21-

[1] It is noted for the record that applicant's election of species (l), "protein," and not species (j), "drug," as the bioactive material necessitates the withdrawal from consideration of claim 60 and its dependents, since claim 60 and its dependents are limited to compositions comprising "drug molecules" and include no embodiments in which a protein is comprised in the composition.

23, 25-33, 39, 48-50, and 52-59 ONLY, to the extent they read on the elected species where applicable.

Information Disclosure Statement

The recitation of references in the specification (as, for example, at page 1, line 16, of the as-filed specification) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892 or by applicant on a proper IDS, they have not been considered.

The information disclosure statement filed 3/19/04 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; **and all other information or that portion which caused it to be listed**. Specifically, the McNally, Benita, Remingtong [*sic*], and USP references are textbooks or reference books for which only portions have been provided, but the listing refers to the entire work in each case; the ExPASy reference is an entire database, but only a few entries have been submitted. A few chapters of the McNally reference are provided. The table of contents only for the Benita reference is provided. A few pages of each of the Remington and USP references have been provided. A few SwissProt entries from the ExPASy database have been provided. The IDS has been placed in the application file, but only the portions of these references submitted by applicant have been considered.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the photographs in Figures 2A and 2B submitted 7/21/04 are dark and grainy. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: The proper name "Remington" is misspelled throughout, *e.g.* at page 7, line 11. Appropriate correction is required.

The abstract of the disclosure is objected to because it is legal rather than narrative in tone and recites numerous phrases that can be implied (for example, "In one embodiment, the present invention is..."). Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Objections

The claims are objected to because the lines are crowded too closely together, making reading difficult. Claims with lines one and one-half or, preferably, **double-spaced** are **required** in all future amendments. See 37 CFR 1.52(b).

Claims 25, 26, 52, and 53 are objected to because of the following informalities: They misspell the word "plasticizer" as "plastificizer." The term "plasticizer" is one of art and is discussed in the specification, for example at page 5, line 22 *et seq.* Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 6, 12, 21-23, 25-33, 39, 48-50, and 52-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a composition with three components: photo-polymerizable monomers ("monomers"), bioactive materials, and an insoluble material with certain properties ("insoluble material"). The claim is incomplete in that it omits essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The claim requires that the bioactive material be "admixed with the monomers" and yet that it be "shielded from the monomers by [the insoluble material]." The manner in which these three components are related within the composition is not clearly pointed out; for

example, it is not clear whether the insoluble material coats the monomers, the bioactive material, both, or neither. It is not clear how two components can be admixed with each other and yet shielded from each other, for example. Clarification is required.

The third component of the composition of claim 1 is "an insoluble material," but the term "insoluble" is relative, and no basis for comparison (*e.g.*, "insoluble in water" or "insoluble in the monomer" or "insoluble in the bioactive material") is provided in the claim. Clarification is required.

Furthermore, claim 1 refers to "body temperature," which is a term that varies depending on the body being measured, *e.g.* a human, an unhealthy human, another mammal, another non-mammalian animal, *etc.* Clarification is required.

Claim 1 is drawn to a product comprising three components, but it includes a limitation regarding the properties of the composition "upon polymerization." Claim 1 also requires that at "body temperature," the insoluble material undergo a change from solid to gel. It is not clear whether the claim means to describe the composition prior to polymerization and/or bringing to body temperature or afterward or both. Clarification is required. The scope of the claim cannot be determined. Specifically, it is not clear whether the solid-gel transition of the insoluble material and/or the polymerization of the monomers are requirements for the instantly claimed composition. The claim should be amended such that the composition being claimed is particularly pointed out.

Finally, claim 1 requires that the bioactive molecules be "protected from attack" after polymerization; it is not clear whether this "attack" is from the monomers (as

implied in line 3 of claim 1) or from another source not recited in the claim. The physical properties implied by this limitation are not clear. Clarification is required.

Because claims 1, 3, 6, 12, 21-23, and 25-31 depend from indefinite claim 1 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 3 provides for the use of the composition of claim 1 "for tissue engineering," but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Furthermore, claim 3 is drawn to a composition, not to a method of using such; therefore, claims to a method *per se* are improper, and submission of method claims may necessitate a second restriction requirement. Clarification is required. If claim 3 is intended to require that the composition of claim 1 be suitable for tissue engineering, it should be amended to read so and should indicate which properties render the composition so suitable.

Claims 21, 25, and 27 require that the composition of claim 1 further comprise a binder, a plasticizer, and a disaggregant, respectively; these claims are incomplete in that they omit essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The claims do not indicate whether the binder, plasticizer, and disaggregant are included with the protein inside the insoluble material shield; whether they are separate entities within the composition; how they relate to the cross-linked structure of

claim 1; and so on. Clarification is required. The claims should be amended to point out the physical and structural relationship of the binder, plasticizer, and disaggregant to the other components of the composition.

Claims 22, 23, 26, and 28 require that the binder, plasticizer, and disaggregant be particular chemical species "or derivatives thereof." The term "derivative" requires only that a particular compound be related in some manner, to some unnamed degree, to the parent compound; by this definition, cellulose is a "derivative of glucose," even though its physical, chemical, and biological properties differ vastly from those of glucose. Elemental carbon is also a "derivative of glucose," since glucose contains carbon. Clarification is required. It is not clear which compounds are considered "derivatives" of the elected species and which are not.

Claim 27 requires that the composition comprise a "disaggregant," which the examiner has interpreted as meaning "an agent that prevents aggregation." This is confusing, however, since claim 1 does not recite any particles that might be prevented from aggregating by the disaggregant of claim 27. Clarification is required.

Claim 29 requires that the bioactive molecules be "shielded by the insoluble material by granulation," which is confusing. It is not clear what is granulated in this claim or how such a physical form might yield protection. Clarification is required.

Claims 32, 48-50, and 52-56 are indefinite for the reasons set forth above regarding claims 1, 21-23, and 25-29, respectively, and for the following reasons where applicable.

Claim 32 is further indefinite in that the second component is "bioactive molecules **previously included in a drug delivery system**." The term "previously" is relative, and no basis of comparison is provided in the claim. It is not clear whether "previously included" requires that a bioactive molecule be one removed from a drug delivery system and included in the instant composition; that it be one that has heretofore been included in a drug delivery system by some artisans within the art; or some other meaning. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 12, 21, 25-29, 32, 39, 48, and 52-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaetsu et al. (1982, U.S. Patent 4,359,483; reference A) taken in light of Sasaki et al. (1991, U.S. Patent 5,047,442; reference B).

Kaetsu teaches a composition comprising insulin ("Component A"), a bioactive protein, encapsulated in cellulose acetate ("Component B," which is insoluble in water, which is itself coated in triethyleneglycol dimethacrylate polymer ("Component C"), (Example 3; column 5, lines 1-29).

Sasaki is cited as evidence that triethyleneglycol dimethacrylate is inherently photopolymerizable (see claim 7 and Example 1).

Claim 3, as discussed above, does not particularly point out the manner in which the composition should be used in tissue engineering; however, the composition of Kaetsu is appropriate for administration to a patient (Abstract and column 1, lines 22-28), so claim 3 is anticipated by Kaetsu. The composition of Kaetsu inherently includes a binder (claims 21 and 48), since the composition is a single membranous capsule and is therefore bound together. The composition of Kaetsu includes cross-linked triethylene glycol dimethacrylate, a natural polymer, and therefore anticipates claims 25-28 and 52-55. Claims 29 and 56, as discussed above, do not particularly point out the nature of the granulation; the composition of Kaetsu is capsules and therefore anticipates these claims. The composition of Kaetsu is a controlled-release composition (claim 57; Abstract and column 1, lines 22-28).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 6, 12, 21, 25-33, 39, 48, and 52-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaetsu et al. (U.S. Patent 4,359,483) taken in view of Sasaki et al. (U.S. Patent 5,047,442)

The teachings of Kaetsu are relied upon as above in the anticipation rejection. Furthermore, Kaetsu teaches that the triethyleneglycol dimethacrylate may be polymerized either by light, for example visible light, or by ionizing radiation (column 3, lines 19-39). Kaetsu also teaches that the insoluble compound ("Component B") may be gelatin (column 2, lines 38-52).

The teachings of Sasaki are relied upon as above.

A person of ordinary skill in the art would have had a reasonable expectation of success in adding a photopolymerization means such as visible light to the composition of Kaetsu because Kaetsu and Sasaki both teach that the triethyleneglycol dimethacrylate ("Component C") in the composition may be polymerized by visible light. The skilled artisan would have been motivated to make such a substitution because Kaetsu teaches that ionizing radiation and visible light are art-accepted equivalents in this art. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

The person of ordinary skill in the art would have had a further reasonable expectation of success in substituting gelatin for cellulose in the composition of Kaetsu because Kaetsu teaches that the encapsulating layer need only comprise a polymer that traps the bioactive component inside the capsules. The skilled artisan would have been motivated to make this substitution because Kaetsu suggests that the two are art-

accepted equivalents. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to include visible light radiation for photopolymerizing the triethyleneglycol dimethacrylate and to substitute gelatin for cellulose in the composition of Kaetsu because Kaetsu suggests including visible light in the composition and substituting gelatin for cellulose.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Claims 22, 23, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaetsu and Sasaki as applied to claims 1, 3, 6, 12, 21, 25-33, 39, 48, and 52-59, above, and further in view of Bar-Shalom et al. (1993, U.S. Patent 5,213,808; reference C).

The teachings of Kaetsu and Sasaki are relied upon as above. Kaetsu and Sasaki are silent as to the inclusion of sugar, in particular the sugars in claims 23 and 50, in the composition.

Bar-Shalom teaches that sugars, for example sucrose, glucose, dextrose, molasses, and lactose, were known in the art at the time of the invention as fillers in controlled-release compositions (column 5, line 32, through column 6, line 34; and column 10, lines 14-59)

A person of ordinary skill in the art would have had a reasonable expectation of success in including a sugar, for example those in claims 23 and 50, in the controlled-release dosage composition of Kaetsu because Bar-Shalom teaches that sugars were well-known fillers in such compositions at the time of the invention. The skilled artisan would have been motivated to include a sugar in the composition of Kaetsu because Bar-Shalom teaches that including fillers improves the bioavailability of drugs in controlled-release compositions (column 7, lines 24-27).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to include sugars, for example those in claims 23 and 50, in the controlled-release dosage composition of Kaetsu because Bar-Shalom teaches that sugars are useful fillers in such compositions.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lora E Barnhart